

RCE of U.S. Serial No.: 09/174,937

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Group Art Unit: 1653

F1 --In another embodiment, a NIP2b, NIP2cL, and NIP2cS of the present invention is identified based on the presence of a "calcium-binding domain" in the protein or corresponding nucleic acid molecule. As used herein, the term "calcium-binding domain" includes a protein domain having an amino acid sequence of about 110 amino acids which has the capacity to bind calcium. Preferably, a calcium binding domain includes a protein domain which is at least 50, 60, 70, 80, 90, or 100 amino acid residues in length and which has the capacity to bind calcium. The calcium-binding domain HMM has been assigned the PFAM Accession MILPAT0063 (Sonnhammer, *et al* (1997) *Proteins* 28:405-420). --

Please replace the paragraph at page 10, lines 11-28 with:

F2 --To identify the presence of a calcium-binding domain in a NIP2b, NIP2cL, or NIP2cS protein, and make the determination that a protein of interest has a particular profile, the amino acid sequence of the protein is searched against a database of HMMs (e.g., the Pfam database, release 2.1) using the default parameters (Sonnhammer, *et al* (1997) *Proteins* 28:405-420). For example, the hmmsf program, which is available as part of the HMMER package of search programs, is a family specific default program for MILPAT0063 and a score of 15 is the default threshold score for determining a hit. Alternatively, the threshold score for determining a hit can be lowered (e.g., to 8 bits). A description of the Pfam database can be found in Sonnhammer *et al.* (1997) *Proteins* 28(3)405-420 and a detailed description of HMMs can be found, for example, in Gribskov *et al.* (1990) *Meth. Enzymol.* 183:146-159; Gribskov *et al.* (1987) *Proc Natl. Acad Sci USA* 84:4355-4358; Krogh *et al.* (1994) *J. Mol. Biol.* 235:1501-1531; and Stultz *et al.* (1993) *Protein Sci.* 2:305-314, the contents of which are incorporated herein by reference. A search was performed against the HMM database resulting in the identification of a calcium-binding domain in the amino acid sequence of NIP2cL (SEQ ID NO: 5) at about residues 55-160 of SEQ ID NO:5 and NIP2cS (SEQ ID NO:8) at about residues 59-96 of SEQ ID NO:8. The results of the searches are set forth in Figures 8 and 9, respectively. --

Please replace the paragraph beginning at page 10, line 33 and ending at page 11, line 11 with:

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F In another embodiment, a NIP2b, NIP2cL, and NIP2cS of the present invention is identified based on the presence of a "4 transmembrane segment integral membrane protein domain" in the protein or corresponding nucleic acid molecule. As used herein, the term "4 transmembrane segment integral membrane protein domain" includes a protein domain having an amino acid sequence of about 50 amino acid residues and having a bit score for the alignment of the sequence to the "4 transmembrane segment integral membrane protein domain" (HMM) of at least 1 or greater. Preferably the term "4 transmembrane segment integral membrane protein domain" includes a protein domain having an amino acid sequence of about 60, 70, 80, or 90 amino acids and having a bit score for the alignment of the sequence to the "4 transmembrane segment integral membrane protein domain" (HMM) of at least 2, preferably 3-10, more preferably 10-30, more preferably 30-50, even more preferably 50-75, 75-100, 100-200 or greater. The "4 transmembrane segment integral membrane protein domain" HMM has been assigned the PFAM Accession PF00335 (Sonnhammer, *et al.* (1997) *Proteins* 28:405-420). A search was performed against the HMM database, as described herein, resulting in the identification of a "4 transmembrane segment integral membrane protein domain" in the amino acid sequence of NIP2b (SEQ ID NO:2) at about residues 253 to 293. The results of the search are set forth in Figure 7.

REMARKS

Claims 1, 2, 4, 5, 8-12, and 27-41 are pending in the application. For the Examiner's convenience all of the pending claims are set forth herein in Appendix A.

Attached hereto is a marked-up version of the changes made to the specification. The attached page is captioned "Version with Markings to Show Changes Made."

No new matter has been added. Any amendments to and/or cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Prolonged And Piecemeal Prosecution Of The Present Case